metastases from patients with breast cancer is significantly increased comparing to the MVD in non-malignant bone tissue when areas of low, medium and highest vascular density were examined (1,8 ±0,71 versus 24,12 ±1,97). Not surprisingly, this difference is even greater, when only hot spots are evaluated.

Conclusions: There is now for the first time evidence of increased microvessel density in bone metastases of patients with breast cancer, which supports the hypothesis of an important role of angiogenesis in bone metastasis. Furthermore, this study suggests, that an antiangiogenic therapy might be an efficacious treatment. Further studies, clarifying the role of angiogenic factors and their receptors in bone metastasis are underway.

Supportive care & quality of life

978 POSTER DISCUSSION

Use and complications of subcutaneous infusion ports. A retrospective study to identify risk factors

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Subcutaneous infusion ports have become important tools in oncological patient care and its use has become standard procedure for long term venous acces. However different complications may arise with its use. The identification of different risk factors may help to reduce their incidence.

We performed a retrospective study on 437 patients, followed at the department of medical oncology and haematology of our institution, in whom an infusion port was inserted between October 1993 and October 1998. All complications were recorded and and a statistical analysis was performed to look for possible predisposing factors.

The main complications were thrombosis (8.46%) and catheter dysfunction (4.86%). Pocket infection and catheter related bacteremia occurred in 4.36% of the cases. Rare complications were: port rotation, catheter disconnection, catheter rupture or kinking, and extravasation.

There was a strong correlation between the anatomical position of the catheter and the incidene of thrombosis and dysfunction. Of those patients in whom the catheter tip was located in the brachiocephalic vein, 45% experienced a thrombotic complication ($p<0.001$). Patients in whom the catheter tip was located in the upper third part of the superior caval vein had thrombosis in 19% of cases ($p<0.01$). In this latter group, port dysfunction rate was 16.7% ($p<0.01$).

This study emphasizes the importance of careful catheter tip positioning in patients with a subcutaneous infusion port. Tightened guidelines and rigorous radiological control after insertion are warranted. A classification in different risk groups according to radiological criteria was proposed. It might serve to select high-risk patients, who could benefit from a prophylactic antithrombotic treatment.

979 POSTER DISCUSSION

Quality of life influenced by primary surgical treatment for stage I-III breast cancer - long-term follow-up of a matched-pair analysis

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Breast conserving therapy has been demonstrated to be just as safe and a less disruptive experience compared to mastectomy for surgically manageable breast cancer. There is, however, no agreement in the literature about the impact of these procedures on several important aspects of quality of life (QoL). The purpose of the present study is to compare the long-term impact of these two surgical approaches on Qol in patients with identical tumor stages and to suggest possible shortcomings of the standard QoL questionnaires.

Between August 1999 and May 2000, QoL questionnaires were answered by 152 pair-matched patients at the I. Frauenklinik, Ludwig-Maximilians University Munich, as part of routine follow-up examinations. The pairs of patients, each consisting of one patient after mastectomy and one after breast conservation, were selected according to the highest degree of equivalence in tumor stage. All patients had been initially treated for stage I-III breast cancer without evidence of distant metastases. The QoL was evaluated by using the QLQ-C30 questionnaire version 2.0 of the EORTC Study Group on Quality of Life. We formulated seven additional questions about the patients' satisfaction with the primary surgical treatment modality as viewed from their current perspective. The QoL questionnaires were answered after a median interval of 46 months following primary treatment.

Tumor stage, prognostic factors, and adjuvant systemic treatment were well balanced between the two groups. No differences between the two groups were observed in terms of all QoL items measured by the QLQ-C30. Our additional questions, however, revealed that patients in the mastectomy group were less satisfied with the cosmetic result of their primary operation ($P< 0.0001$), were more likely to feel basic changes in their appearance ($P< 0.0001$), and were more likely to be emotionally stressed by these facts ($P< 0.0001$). From their perspective at the time of completing the questionnaires, 11 patients in the mastectomy group (15%) would decide differently about the surgical treatment modality, compared to only 3 patients (4%) in the breast conservation group ($P=.025$).

While the primary surgical treatment modality seems to have no long-term impact on the general QoL, certain body image related problems may be caused by mastectomy. Standard measuring instruments for QoL may fail to detect differences in satisfaction and adaptation with the primary surgical treatment modality.

980 POSTER DISCUSSION

Early intervention with epoetin alfa treats anaemia and improves quality of life in ovarian cancer patients undergoing chemotherapy

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Purpose: Anaemia occurs in up to 60% of ovarian cancer patients treated with platinum-based chemotherapy (CT). This randomised, multicentre study investigated the effect of early intervention (haemoglobin (Hb) level: 10-12g/dL) with epoetin alfa during CT to treat and prevent anaemia.

Patients and Methods: 182 patients were randomised 2:1 to receive 10,000 IU epoetin alfa (EPREX/ERYPO, Ortho Biotech/Janssen Cilag) thrice weekly or best standard of care (BST). Patients had confirmed ovarian cancer and a Hb level of ≃12.0g/dL (mean ±SD: 10.69±0.91g/dL). Patients were assessed at six time points during chemotherapy (baseline; 4-6, 8-9, 12, 16-18 and up to 28 weeks) for Hb, Quality of Life (QoL; Functional Assessment of Cancer Treatment - Anaemia (FACT-An), Cancer Linear Analogue Scale (CLAS) and blood transfusion requirements.

Results: Results are presented on 160 patients (mean age±sd: 59.4±11.6 years). At baseline, the groups were balanced for demographic, treatment and disease-related variables (mean Hb±sd: 10.72±0.94g/dL vs 10.63±0.85g/dl, EPO vs BST). Changes in Hb from baseline were significantly greater in the epoetin alfa group than in the BST group at all time points ($p<0.001$). The differences between groups were most marked at 8-9 and 12 weeks (mean±sd: 2.03±1.45g/dl and 2.01±1.15g/dL, respectively). At 12 weeks, 74% of epoetin alfa patients and 11% of BST patients had achieved Hb values >12.0g/dL. Significantly more BST patients required blood transfusions than did those treated with epoetin alfa (16.7% vs 5.7%, $p=0.041$). A within-group analysis of EPO-treated patients showed significant improvements ($p<0.001$) in QoL scores (CLAS: energy, activities and overall QoL) during CT; the average score of all three scales increased by 29% between baseline (55.33±23.13) and last observation (71.32±24.53), with increases of up to 37% seen at 12 weeks. No significant improvements were observed in the BST patients. More detailed analysis, including an across-group comparison of QoL is ongoing.

Conclusions: Early treatment (Hb: 10-12g/dL) with epoetin alfa of ovarian cancer patients undergoing CT significantly increased Hb levels. Hb levels were maintained up to 2g/dL higher in patients receiving epoetin alfa than in those given best standard of care, which reduced the risk of anaemia. Higher Hb levels resulted in fewer blood transfusions and meaningful improvements in QoL.

981 POSTER DISCUSSION

A phase III, double-blind, placebo-controlled, randomized study of novel erythropoiesis stimulating protein (NESP) in patients undergoing platinum-treatment for lung cancer

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Purpose: NESP binds to the erythropoietin (EPO) receptor and stimu-

lates erythropoiesis by the same mechanism as recombinant human EPO (rHuEPO), but has a longer serum t1/2. NESP was shown to be safe and clinically effective in cancer pts when administered every 1, 2, and 3 weeks in phase 1/2 studies. This phase 3 study compared the efficacy of NESP with placebo in lung cancer pts receiving platinum-containing chemotherapy (ctx).

Methods: 320 anemic pts ([Hb] ≤ 11 g/dL) receiving platinum containing ctx (ECOG 0–2, not iron deficient, no rHuEPO therapy within 8 wks or <2 RBC transfusions (tfn) within 4 wks) were randomized to NESP 2.25 μg/kg or placebo (1:1). Study drug was administered SC once weekly (QW) for a maximum of 12 wks (tx phase).

Results: NESP significantly ($p < 0.001$) reduced the Kaplan-Meier proportion (95% CI) of pts transfused during wks 5–12: NESP 21% (15, 28), placebo 51% (43, 60) and during the tx phase (wks 1–12): NESP 26% (20, 33). placebo 60% (52, 68). NESP pts received fewer standard units (mean [SD]) of RBC than placebo pts during wks 5–12: NESP 1.92 (3.27), placebo 0.67 (1.7) and during the tx phase: NESP 2.64 (4.32), placebo 1.14 (2.38). NESP pts were hospitalized fewer mean (SD) days compared with placebo pts (NESP 10.3 [13.5] days, placebo 13.0 [17.7] days). More NESP subjects had a ≥10% increase in the FACT-F scale score than placebo pts ($p = 0.023$) suggesting that NESP decreases fatigue. The safety profile of NESP was similar to placebo and as expected for this population.

Conclusions: NESP 2.25 μg/kg administered QW significantly reduced the proportion of subjects with RBC tfns and was well tolerated. The clinical benefit of NESP was sooner than previously reported for rHuEPO (Abels, 1991) where RBC tfn only reached statistical significance only if the first month of treatment was excluded.

982 POSTER DISCUSSION

Oncologic acute toxicity unit: development of a new tool in the oncologic clinical practice

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Introduction: We have developed an oncologic acute toxicity unit (OATU) in order to attend promptly the specific acute symptoms related to chemotherapy.

Objectives: To analyse the characteristics of patients that contact with the OATU and their outcome.

Patients and methods: Our data set included all the patients receiving chemotherapy in our hospital and the symptoms related to this treatment.

In the first chemotherapy cycle each patient receive an information booklet with the contact phone of the OATU. When patients called, a specialised nurse attended them and she consulted to the medical oncologist if it was necessary. The unit provides access to complementary exams, ambulatory treatment and hospitalisation if it is indicated.

Results: 829 patients established 1465 contacts to the OATU from February 1999 to February 2001. Most common tumours were breast 216 (26%), colorectal 172 (21%) and lung 165 (20%). Most contacts were done by phone (86.5%) and 38.6% were considered inappropriate. From 899 appropriate contacts, the most frequent chemotherapy schedule were 5-FU-Folinic Acid (12.6%) and CMF (11.6%) and the most frequent complaints were fever (35.3%), diarrhoeas (20%), mucositis (15.8%) and emesis (14.5%). 488/899 (54.3%) required attendance to the OATU and 191/488 required hospitalisation (21.2% of the initial appropriated contacts). Grade III/IV neutropenic fever was the most frequent cause of hospital admission (58.1%).

Conclusions: The development of an OATU provides a quick and easy access for patients who suffer acute toxicity related to chemotherapy treatment. In our experience it guaranties a prompt and specialised treatment and avoids unnecessary consults in the Emergency Room. Hospital admission, which was required in 21.2% of appropriate contacts, is therefore optimised.

Paediatric oncology

983 POSTER DISCUSSION

Impact of radiotherapy on survival in supratentorial PNET of childhood: results of the German prospective HIT-trials

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Purpose: To evaluate dose, volume, and sequence of radiotherapy (RX) with respect to progression free survival and pattern of relapse.

Methods: Since 1988 in Germany and Austria children with newly diagnosed malignant brain tumors were enrolled in the multicenter brain tumor trials. In the pilot trial HIT'88/'89 all pts. received immediate postoperative chemotherapy (CX) consisting of 2 cycles of Ifo/VP-16, hdMTX, DDP/Ara-C followed by RX (prescription: 35.2 Gy craniospinal + 20 Gy tumor boost). In the HIT'91 trial pts. were randomized after surgery either to undergo preirradiation CX, or immediate RX followed by maintenance CX (8 x CCNU/VCR/Cis).

Results: 63 children (age 2.9-17.7 months) were eligible. 23 children received maintenance CX, 40 received preirradiation CX. 48 children underwent irradiation according to the guidelines. 7 children were irradiated only locally, in 2 children no RX at all was administered. In 6 children dose was less than 54 Gy to the tumor site, or less than 35 Gy to the neuraxis. Follow-up was 31 months. Overall survival at 3 yrs. was 48.4%. Progression occurred in 38 children with local recurrences in 27 pts. Median time to progression was 10 months. 9 progressions occurred during preirradiation treatment. Dose and volume of RX had significant impact on survival; PFS after 3 years was 49.3% with correct dose and volume of RX as compared to 6.7% for 15 pts. with violations of RX guidelines ($p=0.0001$).

Conclusion: Craniospinal RX is needed to achieve reasonable treatment results in supratentorial PNET in childhood. At least doses of 54 Gy to the tumor, and 35 Gy to the neuraxis are required. The delay of RX seems to increase risk of early progression. Relapses mainly occur at the primary tumor region, but also within the CNS.

984 POSTER DISCUSSION

Dose intensive therapy and myeloablative chemotherapy with haematopoietic stem cell rescue in childhood poor prognosis Ewing's sarcoma

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Purpose: To improve the prognosis of paediatric patients (pts) with high risk Ewing's Sarcoma (HR-ES).

Methods: Previously untreated pts, aged less than 18 years at diagnosis, with newly diagnosed HR-ES of bone because metastatic or localised but with tumour volume more than 100 cm3. Treatment consisted of: induction therapy with two courses of Vincristine (Vcr) 2 mg/m2, Cyclophosphamide (C) 2200 mg/m2 and Adriamicina (Adr) 90 mg/m2 in two days (Hyper-VAdC), alternated to two courses of Etoposide (VP16) 600 mg/m2 in three days plus C 4000 mg/m2 (CE); G-CSF supports each cycle of chemotherapy in order to improve dose intensity and enhance peripheral blood stem cell mobilisation after CE; Surgery and/or Radiotherapy for local control of primary and/or metastatic sites of disease; Maintenance chemotherapy consisting of two courses of Vcr 1,5 mg/m2, C 1200 mg/m2 and Adr 80 mg/m2 in two days (VAdC) alternated with two courses of VP16 500 mg/m2 plus Ifosfamide 9000 mg/m2 in five days (IE). At the end of this phase pts who were not in progression of disease were eligible for consolidation therapy and received Busulfan (Bu) 4 mg/kg/die for 4 days, VP16 800 mg/m2/die for 3 days and Thiotepa (TT) 300 mg/m2 followed by peripheral blood stem cell rescue.

Results: From April 1993 to May 1999, 43 pts 10 with localised and 33 with metastatic disease were enrolled in this protocol. Four pts progressed during the maintenance phase and 34/39 pts eligible were grafted. At time of graft 12 pts were in CR. The median number of CD34+ infused was 6.9 (2.5-40.1)x106/kg. Despite 10 patients received both Bu and total lung irradiation, nor pulmonary toxicity and toxic death related to consolidation procedure were registered. After a median follow up from the diagnosis of 47 (23-89) months, 20/43 patients are in CR, and 2 are alive with disease. The 6 years OS (SE) and PFS (SE) were 48.6% (9.6) and 42.3% (8.3) respectively. Patients with metastasis at diagnosis fared substantially worse than pts with localised disease (6 years PFS 35.8% vs 64.0%, p=.066), moreover pts with bone metastasis (PFS = 14.4%) have a poorer outcome.